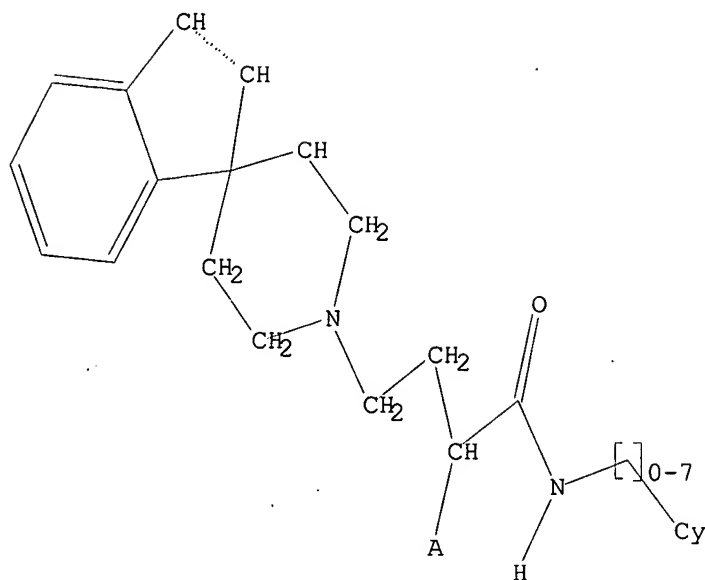


EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	290	546/17.ccls.	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/02/22 13:39
L2	1028	514/278.ccls.	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/02/22 13:39
L3	1173	l1 or l2	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/02/22 13:40
L4	1154	L3	US-PGPUB; USPAT	OR	ON	2007/02/22 13:40



Structure attributes must be viewed using STN Express query preparation.

=> s l1 full

FULL SEARCH INITIATED 13:08:28 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 479 TO ITERATE

100.0% PROCESSED 479 ITERATIONS
SEARCH TIME: 00.00.01

21 ANSWERS

L2 21 SEA SSS FUL L1

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COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

172.10

172.31

FILE 'CAPLUS' ENTERED AT 13:08:31 ON 22 FEB 2007

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L3

2 L2

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L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

DOCUMENT NUMBER:

TITLE:

AUTHOR(S):

CORPORATE SOURCE:

SOURCE:

PUBLISHER:

DOCUMENT TYPE:

LANGUAGE:

GI

2006:830241 CAPLUS

145:327676

4-Amino-2-alkyl-butyramides as small molecule CCR2 antagonists with favorable pharmacokinetic properties
Butora, Gabor; Morriello, Gregori J.; Kothandaraman, Shankaran; Guladeen, Deodialsingh; Pasternak, Alexander; Parsons, William H.; MacCoss, Malcolm; Vicario, Pasquale P.; Cascieri, Margaret A.; Peng, Lihua

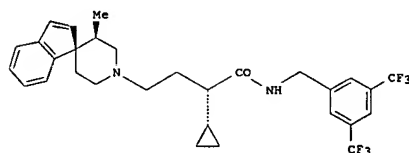
Merck Research Laboratories, Rahway, NJ 07065, USA
Bioorganic & Medicinal Chemistry Letters (2006), 16(18), 4715-4722

CODEN: BMCLE8; ISSN: 0960-894X

Elsevier B.V.

Journal

English



I

AB A systematic examination of the central aromatic portion of the lead (2S)-N-[3,5-bis(trifluoromethyl)benzyl]-2-(4-fluorophenyl)-4-[[1'H-spiro[indene-1,4'-piperidin]-1'-yl]butanamide (9) led to the discovery of a novel class of CCR2 receptor antagonists, which carry small alicyclic groups such as cyclopropyl, cylobutyl, or cyclopropylmethyl attached at

C2 of the carbon backbone. The most potent compound discovered, namely (2S)-N-[3,5-bis(trifluoromethyl)benzyl]-2-cyclopropyl-4-[[1R,3'R]-3'-methyl-1'H-spiro[indene-1,4'-piperidin]-1'-yl]butanamide (I), showed very high binding affinity (IC₅₀ = 4 nM, human monocyte) and excellent selectivity toward other related chemokine receptors. The excellent pharmacokinetic profile of this new lead compound allows for extensive in vivo evaluation.

IT 691874-50-7P 691874-60-9P 691874-61-0P

691874-66-5P 691875-74-8P 691875-75-9P

691875-55-1P 691875-56-2P 691875-57-3P

691875-58-4P 691875-61-9P 691875-62-0P

691875-63-1P 691875-64-2P 691875-65-3P

L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

909717-66-4P 909717-67-5P 909717-73-3P

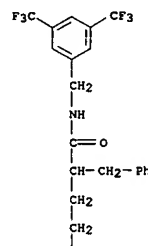
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(amino alkyl butyramides as CCR2 antagonists with favorable pharmacokinetic properties)

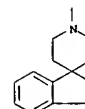
RN 691874-50-7 CAPLUS

CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-α-(phenylmethyl)- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



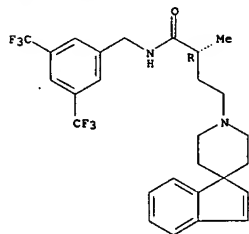
RN 691874-60-9 CAPLUS

CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[[3,5-

L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

bis(trifluoromethyl)phenyl]methyl]-α-methyl-, (αR)- (9CI) (CA INDEX NAME)

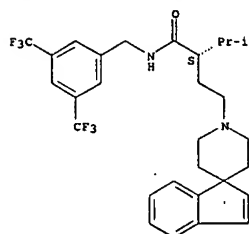
Absolute stereochemistry.



RN 691874-61-0 CAPLUS

CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-α-(1-methylethyl)-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

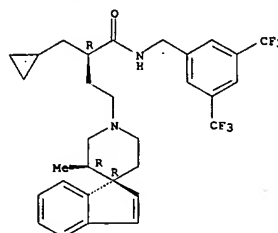


RN 691874-66-5 CAPLUS

CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-α-(cyclopropylmethyl)-3'-methyl-, (αR,1R,3'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

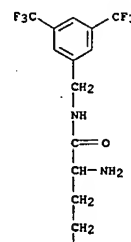
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RN 691875-74-8 CAPLUS

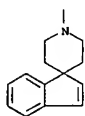
CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, α-amino-N-[[3,5-bis(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



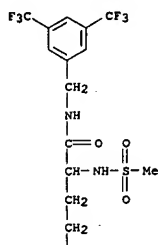
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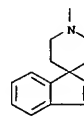
RN 691875-75-9 CAPLUS
 CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[(3,5-bis(trifluoromethyl)phenyl)methyl]-α-[(methylsulfonyl)amino]- (9CI) (CA INDEX NAME)

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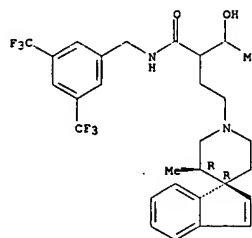
L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 2-A



RN 909717-55-1 CAPLUS
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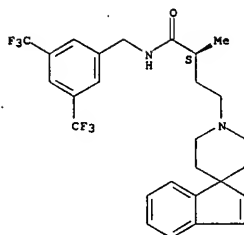
Absolute stereochemistry.



RN 909717-56-2 CAPLUS
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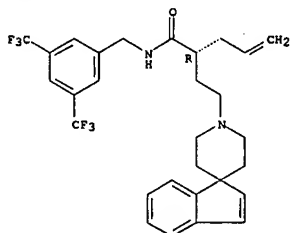
Absolute stereochemistry.

L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 909717-57-3 CAPLUS
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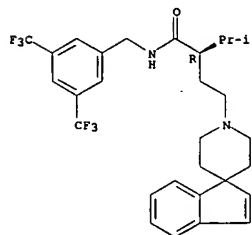
Absolute stereochemistry.



RN 909717-58-4 CAPLUS
 CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[(3,5-bis(trifluoromethyl)phenyl)methyl]-α-(1-methylethyl)-, (αR)- (9CI) (CA INDEX NAME)

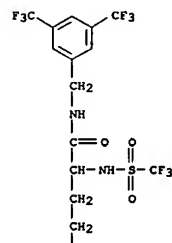
Absolute stereochemistry.

L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 909717-61-9 CAPLUS
 CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[(3,5-bis(trifluoromethyl)phenyl)methyl]-α-1-[(trifluoromethyl)sulfonyl]amino]- (9CI) (CA INDEX NAME)

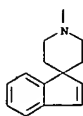
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L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

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RN 909717-62-0 CAPLUS

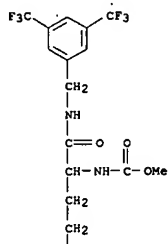
CN Carbamic acid,

[1-[[[3,5-bis(trifluoromethyl)phenyl]methyl]amino]carbonyl

]-3-spiro[1H-indene-1,4'-piperidin]-1'-ylpropyl]-, methyl ester (9CI)

(CA INDEX NAME)

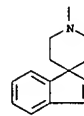
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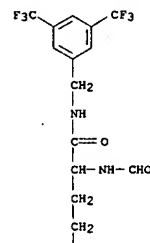
PAGE 2-A



RN 909717-63-1 CAPLUS

CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-α-(formylamino)- (9CI) (CA INDEX NAME)

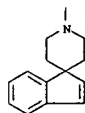
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L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

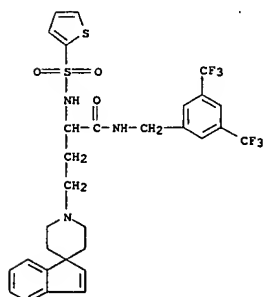
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PAGE 2-A



RN 909717-64-2 CAPLUS

CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-α-[(2-thienylsulfonyl)amino]- (9CI) (CA INDEX NAME)

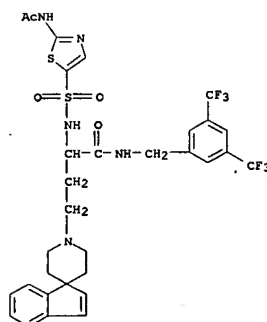


RN 909717-65-3 CAPLUS

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L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

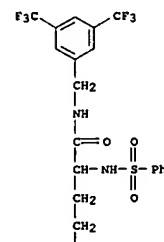
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RN 909717-66-4 CAPLUS

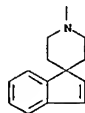
CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-α-[(phenylsulfonyl)amino]- (9CI) (CA INDEX NAME)

PAGE 1-A

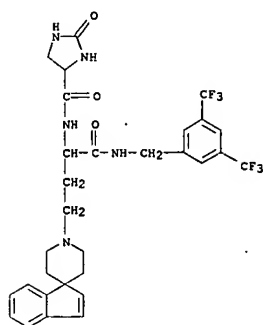


L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

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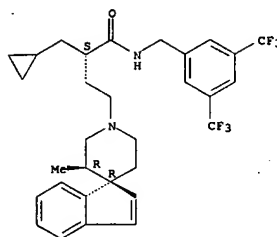
RN 909717-67-5 CAPLUS
 CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[(3,5-bis(trifluoromethyl)phenyl)methyl]-α-[(2-oxo-4-imidazolidinyl)carbonyl]amino- (9CI) (CA INDEX NAME)



RN 909717-73-3 CAPLUS
 CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[(3,5-bis(trifluoromethyl)phenyl)methyl]-α-(cyclopropylmethyl)-3'-methyl-, (αS,1R,3'R)- (9CI) (CA INDEX NAME)

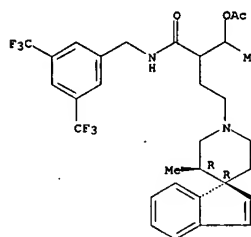
Absolute stereochemistry.

L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



IT 909717-54-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (amino alkyl butyramides as CCR2 antagonists with favorable pharmacokinetic properties)
 RN 909717-54-0 CAPLUS
 CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, α-[(1-(acetyloxy)ethyl)-N-[(3,5-bis(trifluoromethyl)phenyl)methyl]-3'-methyl-, (1R,3'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:412814 CAPLUS
 DOCUMENT NUMBER: 140:423589
 TITLE: Preparation of piperidinylbutyramides and related compounds as modulators of CCR-2 chemokine receptor activity
 INVENTOR(S): Butora, Gabor; Pasternak, Alexander; Yang, Lihu; Zhou, Changyou
 PATENT ASSIGNEE(S): Merck & Co., Inc., USA
 SOURCE: PCT Int. Appl., 239 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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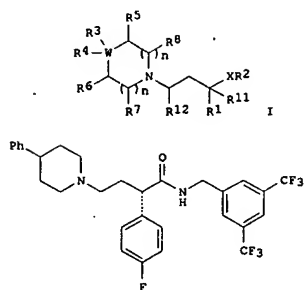
OTHER SOURCE(S): MARPAT 140:423589
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L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 1-A



II

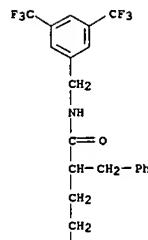
AB Title compds. [I; W = C, N, O; X = NR10, O, CH2O, CONR10, CO2, etc.; R10 = H, (substituted) alkyl, Ph, PhCH2, alkyl, cycloalkyl; R1 = H, (substituted) alkyl-Y-Ph, alkyl-Y-heterocyclyl, etc.; Y = bond, O, S, SO2, NR10; R2 = (substituted) alkylphenyl, alkylheterocyclyl; R3 = H, (substituted) alkylphenyl, alkylheterocyclyl, CF3, cycloalkyl, etc.; R4 = H, OH, alkyl, alkoxy, cyano, etc.; R3R4 = atoms to form (substituted) indene, benzofuran, isobenzofuran, benzothiofuran, isobenzofuran rings; R5-R8 = H, OH, alkyl, alkoxy, O, halo, CF3, CO2R9, etc.; R9 = H, (substituted) alkyl, cycloalkyl, Ph, PhCH2; R3R5, R4R6, R5R6, R7R8 = atoms to form (substituted) rings; R11 = H, halo, alkyl, OH, alkoxy, NR9R10, etc.; R12 = H, alkyl, CO2R9; n = 0-3], were prepared Thus, title compound (II) was prepared by reaction of 4-phenylpiperidine with the corresponding aldehyde in the presence of Na(OAc)3BH. I bound to CCR-2 receptor with IC50 ≤ 1 μM.

IT 691874-50-7P 691874-52-9P 691874-60-9P
691874-61-0P 691874-66-5P 691875-72-6P
691875-74-8P 691875-75-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

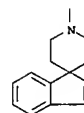
(reparation of piperidinybutyramides and related compds. as modulators of CCR-2 chemokine receptor activity)

RN 691874-50-7 CAPLUS
CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-α-(phenylmethyl)- (9CI) (CA INDEX NAME)



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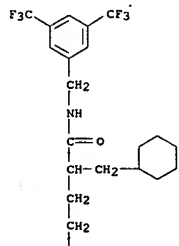
RN 691874-52-9 CAPLUS
CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-α-(cyclohexylmethyl)- (9CI) (CA INDEX NAME)



L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

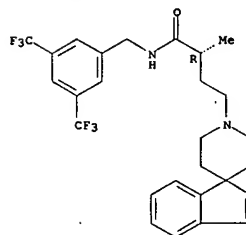
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PAGE 2-A

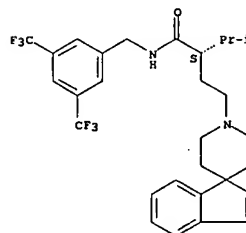
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CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-α-methyl-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 691874-61-0 CAPLUS
CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-α-(i-methylethyl)-, (αS)- (9CI) (CA INDEX NAME)

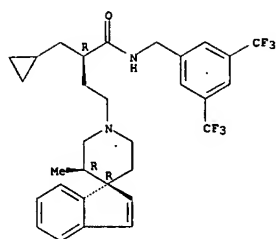
Absolute stereochemistry.



RN 691874-66-5 CAPLUS
CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-α-(cyclopropylmethyl)-3'-methyl-, (αR,1R,3'R)- (9CI) (CA INDEX NAME)

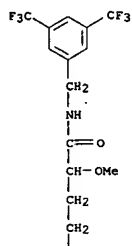
Absolute stereochemistry.

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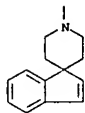
RN 691875-72-6 CAPLUS
 CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-((3,5-bis(trifluoromethyl)phenyl)methyl)-α-methoxy- (9CI) (CA INDEX NAME)

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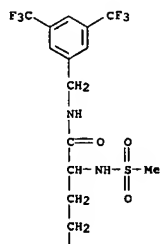
L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

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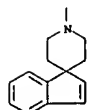


RN 691875-75-9 CAPLUS
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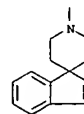
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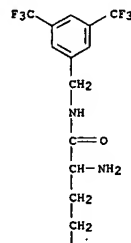


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RN 691875-74-8 CAPLUS
 CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, α-amino-N-((3,5-bis(trifluoromethyl)phenyl)methyl)- (9CI) (CA INDEX NAME)

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